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Evaluation of Inhaled Low Dose Formaldehyde Induced DNA Damage by Liquid Chromatography-Tandem Mass Spectrometry (#633)

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As a high volume chemical, formaldehyde toxicity and carcinogenesis have been controversial. Previously, we have demonstrated that exogenous formaldehyde induced DNA monoadducts accumulate in a highly nonlinear manner. However, the effect of low dose exogenous formaldehyde exposure in the range of regulatory limit values is still unclear. In this study, both exogenous and endogenous DNA monoadduct (N2-HOMe-dG) and DNA-protein crosslink (DPC, dG-Me-Cys) were measured to assess the accumulation of DNA adducts arising from the inhalation to 0, 1, 30, 300 ppb [13C2H2]-formaldehyde for 28 days (6 hours/day). Ultrasensitive nano-liquid chromatography mass spectrometry, including triple quadruple and high resolution Orbitrap mass spectrometer, was used to improve the sensitivity and detection of DNA monoadducts and DPC. Our data clearly show that low exogenous formaldehyde exposure did not cause detectable amounts of exogenous DNA monoadducts or DPC in any tissue of exposed rats. In contrast, endogenous formaldehyde adducts were detectable in all tissues analyzed, with mean levels ranging from 2.35 to 5.06 adducts per 107 dG and 1.52 to 8.03 adducts per 108 dG for DNA monadducts and DPC in different tissues, respectively. These novel findings substantiate the threshold mode of action of carcinogenesis and will further improve risk assessment of low formaldehyde exposures in the range of regulatory limit values.

Keywords: Formaldehyde, carcinogenesis, DNA-adducts, risk assessment